

Is BMI a Factor in Compliance to Adjuvant Chemotherapy for Locally Advanced Rectal Cancer?

A multicenter retrospective analysis and comparison with non-obese patients

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Rezumat

Este IMC un factor care contribuie la respectarea indicațiilor de chimioterapie adjuvantă în cazul cancerului rectal local avansat?

O analiză retrospectivă multicentrică și o comparație cu pacienți normoponderali

Context: Respectarea indicațiilor de chimioterapie adjuvantă în cazul pacienților supuși intervențiilor chirurgicale rectale variază între 43% și 73,6%. Motivele pentru care nu s-a început sau nu s-a finalizat chimioterapia adjuvantă cuprind apariția complicațiilor postoperatorii, toxicitatea medicamentoasă, progresia bolii și/sau preferințele pacientului. Nu se cunosc multe despre impactul obezității asupra respectării indicațiilor de chimioterapie adjuvantă în acest context.

Metode: Acest studiu retrospectiv, multicentric, a analizat respectarea indicațiilor de chimioterapie adjuvantă și morbiditatea asociată tratamentului în cazul a 511 pacienți care au suferit o intervenție chirurgicală curativă pentru cancer rectal în șase centre din Italia specializate în tratamente pentru afecțiuni colorectale, în perioada ianuarie 2013 - decembrie 2017.

Rezultate: 70 dintre pacienți erau obezi (IMC > 30 kg/m²). Proportia procedurilor chirurgicale deschise (22,9% vs. 13,4%) și a

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conversiilor (14,3% vs. 4,8%) a fost mai mare în cazul pacienților obezi, comparativ cu cei normoponderali ($p < 0,001$). Durata medie a spitalizării a fost cu o zi mai mare în cazul pacienților obezi (9 zile vs. 10 zile, $p = 0,038$), fără a exista vreo diferență semnificativă din punct de vedere statistic în ceea ce privește rata complicațiilor, atât în general (58,6% în cazul pacienților obezi vs. 52,3% în cazul celor normoponderali), cât și prin prisma scorului Clavien-Dindo ≥ 3 (17,1% vs. 10,9%). S-au oferit indicații de chimioterapie adjuvantă pentru 49/70 (70%) de pacienți din grupul cu pacienți obezi și pentru 306/441 (69,4%) de pacienți din grupul de pacienți normoponderali ($p = 0,43$). Nu a existat o diferență semnificativă din punct de vedere statistic în ceea ce privește respectarea indicațiilor de chimioterapie adjuvantă: 18,4% dintre pacienții obezi, respectiv 22,9% dintre cei normoponderali nu au început chimioterapia adjuvantă, în vreme ce 36,7%, respectiv 34,6% au început-o, însă nu au finalizat tratamentul programat ($p = 0,79$). Per total, 55% dintre pacienții care au început chimioterapia adjuvantă au finalizat cu succes tratamentul.

Concluzii: Obezitatea nu a influențat respectarea indicațiilor de chimioterapie adjuvantă în cazul cancerului rectal local avansat: gradul de respectare a indicațiilor a fost redus atât în cazul pacienților obezi, cât și în cel al pacienților normoponderali, fără să existe vreo diferență majoră din punct de vedere statistic între cele două grupuri. Rata complicațiilor majore nu a fost influențată semnificativ din punct de vedere statistic de nivelul ridicat al IMC.

Cuvinte cheie: cancer rectal, obezitate, chimioterapie adjuvantă

Abstract

Background: Compliance to adjuvant chemotherapy (AC) for patients undergoing rectal surgery ranges from 43% to 73.6%. Reasons reported for not initiating or completing AC include onset of postoperative complications, drug toxicity, disease progression and/or patient preferences. Little is known regarding the impact of obesity on the compliance to AC in this setting.

Methods: This multicenter, retrospective study analyzed compliance to AC and treatment-related morbidity in 511 patients having undergone surgery with curative intent for rectal cancer in six Italian colorectal centers between January 2013 and December 2017.

Results: 70 patients were obese (BMI > 30 kg/m²). The proportion of open procedures (22.9% vs. 13.4%) and conversions (14.3% vs. 4.8%) was greater in obese compared to non-obese patients ($p < 0.001$). Median hospital stay was one day longer for obese patients (9 days vs. 10 days, $p = 0.038$) while there was no statistically significant difference in the complication rate, whether overall (58.6% in obese vs. 52.3% in non-obese) or with a Clavien-Dindo score ≥ 3 (17.1% vs 10.9%). AC was offered to 49/70 (70%) patients in the obese group and 306/441 (69.4%) in the non-obese group ($p = 0.43$). There was no statistically significant difference in AC compliance: 18.4% and 22.9% did not start AC, while 36.7% and 34.6%, started AC but did not complete the scheduled treatment ($p = 0.79$) in the obese and non-obese group, respectively. Overall, 55% of patients who started AC successfully completed their adjuvant treatment.

Conclusions: Obesity did not impact compliance to AC for locally advanced rectal cancer: compliance was poor in obese and non-obese patients with no statistically significant difference between the two groups. Major complication rate was not statistically significantly affected by increased BMI.

Key words: rectal cancer, obesity, adjuvant chemotherapy

Introduction

Adherence to adjuvant chemotherapy (AC)

schedules for patients who undergo rectal surgery for cancer have been reported to range from 43% to 73.6% (1,2). The main reported

reasons for not initiating or completing adjuvant therapy included the onset of post-operative complications, drug intolerance, disease progression, and patient preference (3).

The prevalence of obesity (as determined by body mass index (BMI) > 30 kg/m²) continues to increase worldwide and in Europe (4). There is increasing data that obesity could be associated with increased risk for various cancers including rectal cancer, especially in male patients (4,5).

Several studies have reported an association between obesity and oncologic outcomes in rectal cancer after AC, but few have studied the relationship between obesity and compliance to AC for locally advanced rectal cancer (6-9).

The main aim of this retrospective multicenter study was to evaluate the impact of obesity on the compliance to AC in a cohort of locally advanced rectal cancer patients undergoing surgical intervention with curative intent. The secondary goals of this study were to analyze the peri-operative complication rates and the reasons for interruption of AC.

Methods

Study population and outcomes

This retrospective cohort study included all consecutive patients who underwent surgery with curative intent for rectal cancer in six Italian colorectal centers between January 2013 and December 2017 (5 years). Patients with stage IV disease, younger than 18 years or undergoing palliative or emergency surgery were excluded from the analysis. Prospectively collected data were entered into a database specifically designed to investigate the compliance to AC. Recorded parameters included patient characteristics, patient frailty as per the Charlson comorbidity index (CCI) (10) and Robinson Score (11), pre-operative tumor stage, neo-adjuvant chemo-radiation therapy, surgical, intra-operative and post-operative parameters, early and delayed surgical complications and administration of AC. We specifically concentrated on the reasons why patients did not start, discontinued or had a modification in their AC regimen.

Failure was considered when AC was not started or was discontinued, when the dose was reduced, or another regimen was started due to intolerance. Obesity was defined as a BMI >30 kg/m². Data were analyzed according to four categories: underweight or normal weight (BMI <25.0 kg/m²), over weight (BMI 25.0–29.9 kg/m²), obesity class I (BMI 30.0–34.9 kg/m²), obese classes II (BMI 30.0 – 35.0 kg/m²) III (BMI 35.0 – 40.0 kg/m²). This study was approved by the local ethical committee of each hospital.

The decision to propose neo-adjuvant and/or adjuvant CT was reached during a multidisciplinary assessment for each patient according to the National Comprehensive Cancer Network® guidelines (12). Surgery was performed 6-8 weeks after completion of neoadjuvant radiation therapy. All patients underwent either total (TME) or partial mesorectal excision depending on the location of the primary tumor. The surgical approach (open versus laparoscopic) was chosen according to surgeons' preference and expertise. A loop ileostomy was planned before surgery based on the distance of the anastomosis from the anal verge, the use of neo-adjuvant chemo-radiation therapy (nCRT) and general health of the patient. Postoperative morbidity was rated according to the Clavien-Dindo (CD) classification (13). Major complications were defined as complications with a CD grade equal to or greater than 3. Three to four weeks after surgery, patients received AC (FOLFOX or CapeOX) for 6 months.

Statistical Analysis

Continuous data were reported as median and interquartile ranges (IQR) and categorical data as numbers and percentages (%).

The chi-square test (or Fisher's exact test when appropriate) and Wilcoxon test were used, to compare categorical and continuous variables between groups, respectively.

Univariate and multivariate log-binomial regression models were performed to evaluate whether obesity status and other selected risk factors were associated with

the risk of major complications (CD score ≥ 3).

A p value < 0.05 was considered statistically significant. All analyses were performed with SAS software, version 9.4 (SAS Institute, Cary, NC).

Results

Of 511 patients corresponding to the inclusion criteria, 441 patients had a BMI less than 30 kg/m², while 70 patients were obese (BMI >30 kg/m²). Patient and tumor related characteristics as well as operative details are reported in *Table 1*. There were no statistically significant

Table 1. Patients characteristics (N=511)

		Not obese PTs (n=441)	Obese PTs (n=70)	p ¹
Age, median (IQR)		71 (62, 78)	69 (60, 75)	0.21
Charlson score, median (IQR)		5 (4, 6)	5 (3, 7)	0.98
Number of lymphnodes, median (IQR)		17 (13, 24)	18 (14, 26)	0.13
	Missing	3	0	
Number of positive lymphnodes (in N+), median (IQR)		3 (1, 4)	1 (1, 3)	0.10
Number of positive mesorectum lymphnodes (in N+), median (IQR)		2 (1, 4)	1 (1, 2)	0.21
BMI classes, n (%)	Underweight (<18.5 kg/m ²)	10 (2.3)	-	-
	Normal weight (18.5 - <25 kg/m ²)	236 (53.5)	-	
	Overweight (25 - <30 kg/m ²)	195 (44.2)	-	
	Obesity class I (30 - <35 kg/m ²)	-	57 (81.4)	
	Obesity class II (35 - <40 kg/m ²)	-	10 (14.3)	
	Obesity class III (≥ 40 kg/m ²)	-	3 (4.3)	
Sex, N (%)	Female	178 (40.4)	26 (37.1)	0.70
	Male	263 (59.6)	44 (62.9)	
Tumor site, n (%)	Low	185 (42.0)	26 (37.1)	0.11
	Middle	177 (40.1)	24 (34.3)	
	High	79 (17.9)	20 (28.6)	
Stage, n (%)	0	3 (0.7)	1 (1.4)	0.27
	Complete response	28 (6.3)	3 (4.3)	
	I	141 (32.0)	20 (28.6)	
	IIA	88 (20.0)	18 (25.7)	
	IIB	8 (1.8)	0 (0.0)	
	IIC	0 (0.0)	1 (1.4)	
	IIIA	41 (9.3)	6 (8.6)	
	IIIB	112 (25.4)	17 (24.3)	
	IIIC	20 (4.5)	4 (5.7)	
Neo-adjuvant CT, n (%)	No	239 (54.8)	38 (55.9)	0.97
	Yes	197 (45.2)	30 (44.1)	
	Missing	5	2	
Tumor type, n (%)	Adenocarcinoma	420 (95.2)	67 (95.7)	1.00
	Mucinous	21 (4.8)	3 (4.3)	
Not sure the next two are needed				
Tumor grade, n (%) ref/	G1	44 (11.4)	7 (12.3)	0.28
	G2	278 (72.2)	36 (63.2)	
	G3	63 (16.4)	14 (24.6)	
	Missing	56	13	
Mismatch repair, n (%)	Absent	44 (19.7)	4 (13.3)	0.55
	Present	179 (80.3)	26 (86.7)	
	Missing	218	40	
Type of surgery, n (%)	Open	59 (13.4)	16 (22.9)	<0001
	Laparoscopic	361 (81.9)	44 (62.9)	
	Conversion	21 (4.8)	10 (14.3)	
Free distal margin, n (%)	No	8 (1.8)	1 (1.4)	1.00
	Yes	433 (98.2)	69 (98.6)	
Free circumference margin, n(%)	No	31 (7.0)	4 (5.7)	0.88
	Yes	410 (93.0)	66 (94.3)	
Ileostomy, n (%)	No	183 (41.5)	36 (51.4)	0.15
	Yes	258 (58.5)	34 (48.6)	

PT: patient; CT:chemotherapy; ¹Chi-square p-value for categorical variables, Wilcoxon p-value for continuous variables

differences between the two groups in CCI, Robinson Score, sex, tumor site, tumor grade and stage (*Table 2*). Retrieved lymph nodes rates as well as the oncological quality of the pathological specimens were adequate in both groups. The proportion of open procedures and conversions was greater in obese (22.9% and 14.3%) compared to non-obese patients (13.4% and 4.8%, $p < 0.001$). Median hospitalization was one day longer for obese patients (9 days vs. 10 days, $p = 0.038$) while there were no statistically significant differences in the complication rates, whether overall (58.6% in obese vs. 52.3% in non-obese) or with a Clavien-Dindo score ≥ 3 (17.1% vs. 10.9%) as reported in *Table 2*.

AC was offered to 49/70 (70%) of the obese patients and to 306/441 (69.4%) of non-obese patients ($p = 0.43$). Reasons for not starting or not completing AC are described in *Table 3*. There was no statistically significant difference in AC compliance: 18.4% and 22.9% did not start, while 36.7% and 34.6%, started but did not complete the scheduled treatment ($p = 0.79$) in the obese and non-obese groups, respectively. Overall, 55% of patients who started AC successfully completed their adjuvant treatment. These results did not change even after stratification of BMI subgroups (*Table 4*).

From log-binomial regression analysis, nCRT, male sex and CCI emerged as risk factors for the onset of major post-operative

complications for obese patients (*Table 5*).

There was no statistically significant difference in the reasons affecting compliance to AC between the two groups: 18% (9/49) obese vs. 22% (70/306) of non-obese patients did not start AC. Stoma related symptoms such as dehydration did not differ statistically significantly between the two groups: 12.8% in the obese vs. 14.6% in the non-obese ($p = 1.00$).

Discussion

The results of our study suggest that obesity does not affect compliance to AC in patients undergoing surgery with curative intent for non-metastatic rectal cancer. No statistically significant difference was found in the complication rate between obese and non-obese patients.

The association between obesity and oncological outcomes has been investigated in other types of cancer, and was found to be associated with higher rates of local recurrence, distant metastasis, and decreased overall survival (14,15). Conversely, other studies described a better survival in obese patients compare to normal weight subjects, possibly due to increased tolerance to peri-operative chemotherapy (16). Weight loss during cancer-related treatment may in fact be better tolerated by overweight subjects, avoiding the typical comorbidities derived from weakened

Table 2. Association between obesity status of patients and outcomes of interest (N=511)

		Not obese PTs (n=441)	Obese PTs (n=70)	p ¹
Days of hospitalization, median (IQR)		9 (6, 13)	10 (7, 16)	0.038
Clavien-Dindo, N (%)	0	208 (47.2)	29 (41.4)	-
	1	110 (24.9)	14 (20.0)	
	2	75 (17.0)	15 (21.4)	
	3a	10 (2.3)	4 (5.7)	
	3b	28 (6.3)	5 (7.1)	
	4a	1 (0.2)	1 (1.4)	
	4b	0 (0.0)	2 (2.9)	
	5	9 (2.0)	0 (0.0)	
Relevant complications, N (%)	No	208 (47.2)	29 (41.4)	0.29
	Minor	185 (42.0)	29 (41.4)	
	Major	48 (10.9)	12 (17.1)	
CT compliance, N (%)	Not indicated	135 (30.6)	21 (30.0)	0.92
	Indicated, but not started	70 (15.9)	9 (12.9)	
	Started, but not completed	106 (24.0)	18 (25.7)	
	Completed	130 (29.5)	22 (31.4)	

PT: patient; CT: chemotherapy; ¹Chi-square p-value for categorical variables, Wilcoxon p-value for continuous variables

Table 3. Reasons for not starting or not completing adjuvant chemo-therapy

	Not obese PTs (N=306)	Obese PTs (N=49)	P ¹
AC started, N (%)			0.58
No	70 (22.9)	9 (18.4)	
Yes	236 (77.12)	40 (81.6)	
Reasons for not starting AC, N (%) ²			
Age	48 (15.7)	6 (12.2)	0.67
Complications	10 (3.3)	4 (8.2)	0.11
General conditions	52 (17.0)	6 (12.2)	0.53
Patient choice	6 (2.0)	0 (0.0)	1.00
AC completed, N (%) ³			1.00
No	106 (44.9)	18 (45.0)	
Yes	130 (55.1)	22 (55.0)	
Changes in AC regimen, N (%) ²			
Shortened	55 (23.3)	6 (15.0)	0.31
Dose lowered	62 (26.3)	9 (22.5)	0.70
Change of AC agent	30 (12.7)	6 (15.0)	0.62
Other events N (%) ²			
Readmission	33 (14.2)	2 (5.1)	0.19
AC where surgery performed	179 (76.5)	31 (77.5)	1.00
Ileostomy closed before AC	23 (10.2)	3 (7.9)	1.00
Dehydration	34 (14.6)	5 (12.8)	1.00
Ileus	9 (3.9)	0 (0.0)	0.37
Mechanical occlusion	5 (2.1)	0 (0.0)	1.00
Ileostomy prolapse	8 (3.4)	0 (0.0)	0.61
Incisional hernia	15 (6.4)	3 (7.7)	0.73
Late anastomotic leak	4 (1.7)	0 (0.0)	1.00
Infection	32 (13.7)	1 (2.6)	0.06
AC toxicity	101 (43.3)	16 (41.0)	0.86

PT: patient; AC: adjuvant chemotherapy; ¹Fisher exact p-value; ²Multiple answers are possible; ³Based on number of PTs who started AC

Table 4. Association between obesity status of patients and outcomes of interest (N=511)

		Underweight or normal weight PTs (N=246)	Over weight PTs (N=195)	Obese I PTs (N=57)	Obese II/III PTs (N=13)	P ¹
Days of hospitalization, median (IQR)		9 (7, 14)	8 (5, 13)	10 (8, 16)	8 (7, 16)	0.41
	Missing	1	1	0	0	
Clavien-Dindo, N (%)	0	123 (50.0)	85 (43.6)	24 (42.1)	5 (38.5)	-
	1	57 (23.2)	53 (27.2)	9 (15.8)	5 (38.5)	
	2	40 (16.3)	35 (17.9)	14 (24.6)	1 (7.7)	
	3a	4 (1.6)	6 (3.1)	4 (7.0)	0 (0.0)	
	3b	16 (6.5)	12 (6.2)	5 (8.8)	0 (0.0)	
	4a	0 (0.0)	1 (0.5)	1 (1.8)	0 (0.0)	
	4b	0 (0.0)	0 (0.0)	0 (0.0)	2 (15.4)	
	5	6 (2.4)	3 (1.5)	0 (0.0)	0 (0.0)	
Grade of complications, N (%)	No	123 (50.0)	85 (43.6)	24 (42.1)	5 (38.5)	0.22
	Minor (<3)	97 (39.4)	88 (45.1)	23 (40.4)	6 (46.2)	
	Major (>2)	26 (10.6)	22 (11.3)	10 (17.5)	2 (15.4)	
CT compliance, N (%)	Not indicated	71 (28.9)	64 (32.8)	15 (26.3)	6 (46.2)	0.30
	Indicated, but not started	46 (18.7)	24 (12.3)	8 (14.0)	1 (7.7)	
	Started, but not completed	61 (24.8)	45 (23.1)	15 (26.3)	3 (23.1)	
	Completed	68 (27.6)	62 (31.8)	19 (33.3)	3 (23.1)	

PT: patient; CT: chemo-therapy; ¹P-value from logistic regression for ordinal response

immune systems (17). With regard to rectal cancer, only few studies (5,6) reported an association between obesity and oncologic outcomes in rectal cancer, and even fewer inquired the relationship between obesity and compliance to AC for locally advanced rectal cancer (18).

Compliance to AC is known to be affected by the rate of peri-operative complications and conversion to open surgery rate since they could translate into a possible delay in adjuvant chemotherapy onset and therefore a possible reduction of completion rate.

Of note in our study is the alarming low

Table 5. Association between patient characteristics and onset of major (Clavien-Dindo score > 2) complications according to log-binomial univariable regression analysis (N=511)

Variable		n. of relevant complications / N tot	%	RR	95% CI	P
All PTs		60/511	12			
Age (years)	+ 10 years			1.12	0.91-1.39	0.29
Charlson score	+ 2 points			1.30	1.07-1.58	0.009
Obesity status ¹	No obese PTs	48/441	11	1.00		
	Obese PTs	12/70	17	1.57	0.88-2.81	0.12
Obesity status ²	Underweight or normal weight	26/246	11	1.00		
	Over weight	22/195	11	1.07	0.62-1.82	0.81
	Obesity class I	10/57	18	1.66	0.85-3.24	0.14
	Obesity class II/III	2/13	15	1.46	0.39-5.48	0.58
Sex	Female	15/204	7	1.00		
	Male	45/307	15	1.99	1.14-3.48	0.015
Tumor site	Low	27/211	13	1.00		
	Middle	25/201	12	0.97	0.58-1.62	0.91
	High	8/99	8	0.63	0.30-1.34	0.23
Tumor stage	0	6/35	17	1.00		
	I	18/161	11	0.65	0.28-1.52	0.32
	II	14/115	12	0.71	0.30-1.71	0.44
	III	22/200	11	0.64	0.28-1.47	0.29
Neo-adjuvant CT	No	23/277	8	1.00		
	Yes	37/227	16	1.96	1.20-3.20	0.007
	Missing	0/4	0	-		
Tumor type	Adenocarcinoma	56/487	11	1.00		
	Mucinous	4/24	17	1.45	0.57-3.67	0.43
Tumor grade	G1	7/51	14	1.00		
	G2	25/314	8	0.58	0.26-1.27	0.17
	G3	15/77	19	1.42	0.62-3.24	0.41
	Missing	13/69	19	-		
Mismatch repair	Absent	5/48	10	1.00		
	Present	16/205	8	0.75	0.29-1.94	0.55
	Missing	39/258	15	-		
Type of surgery	Open	14/75	19	1.00		
	Laparoscopic	39/405	10	0.52	0.30-0.90	0.02
	Conversion	7/31	23	1.21	0.54-2.71	0.64
Free distal margin	No	2/9	22	1.00		
	Yes	58/502	12	0.52	0.15-1.81	0.30
Free circumference margin	No	7/35	20	1.00		
	Yes	53/476	11	0.56	0.27-1.13	0.11
Ileostomy	No	24/219	11	1.00		
	Yes	36/292	12	1.12	0.69-1.83	0.63

RR: relative risk; CI: confidence interval; PT: patient; CT: chemotherapy; ^{1,2}Obese status into two categories: AIC = 371.63, logL = -183.81; obese status into four categories: AIC = 375.54, logL = -183.77. p-value LRT (2 gdl) = 0.96

rate of full compliance to adjuvant treatment in patients operated for locally advanced rectal cancer, whether the patients were obese or not, confirming the data already reported in the literature regarding inadequate adherence to AC (21,22). Notwithstanding, our overall 55% adherence rate compares favorably with the literature. Forty-three% of patients who were randomized to receive postoperative chemotherapy finally received the planned dose within the scheduled time interval. More than a quarter of patients could not even start adjuvant chemotherapy due to postoperative

complications, absence of tumour resection, disease progression, or patient refusal). Unsatisfactory compliance to AC does not seem to be related to the type of patients receiving the treatment (23). The role of neoadjuvant therapy (24) should be taken into consideration to improve compliance in patients with locally advanced rectal cancer.

The main causes of incomplete AC did not differ significantly between the two groups. The data we found are quite in line with those reported in the literature (21,22). Patient age is no longer considered as an absolute

contraindication to adjuvant chemotherapy (25), while post-operative complications and general conditions have excluded a considerable number of patients from adjuvant therapy.

Chemotherapy toxicity and patient dehydration (mainly due to increased ostomy output) were found to be the main factors of deteriorated compliance to AC, similar to what was observed in the EORCT (21) and Chronicle (22) trials, but the BMI of patients in these two randomized studies was not detailed.

We found that obese patients treated with nCRT were at higher risk for the onset of post-operative complications (overall and major complications (Clavien-Dindo ≥ 3). This result could be explained by the technical difficulty of operating obese patients with irradiated pelvis compared to non-obese patients. Interestingly, this increase in the complication rate did not translate into a reduced compliance to AC.

The poor compliance to AC in our reported population undergoing surgery for rectal cancer suggests that a change in treatment should be implemented moving towards a totally neo-adjuvant therapy setting.

Our study has several limitations. Data were reviewed and analyzed retrospectively; the obese group is substantially smaller than the non-obese group. Moreover, we did not study oncological outcomes such as disease-free survival and overall survival. Our aim was to study the actual compliance of obese patients to AC after rectal cancer surgery, as we believe this information is missing from the current literature, and may be one of importance for daily clinical practice, and in particular, for patient information.

Conclusion

Obesity did not impact compliance to adjuvant chemotherapy for locally advanced rectal cancer: compliance was quite poor in both obese and non-obese patients. Increased BMI was not associated with increased major complications, while pre-operative chemoradiation therapy was found to be a risk factor

for developing major complications in obese patients.

Conflict of Interest

All authors declare that they have not hing to disclose.

Ethics Approval

The study was approved by the local ethics committee of the each hospitals.

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